

CLAIMS

1. (original): A pellet which is adapted for use as a core for a pharmaceutical dosage form, said pellet having an inner and an outer zone, said inner zone comprising a biologically active agent and said outer zone comprises a layer which is formed by applying to said inner zone, a substantially dry, free flowing inert powder which forms a non-tacky surface when placed in contact with water.

2. (original): A pellet as defined in claim 1 wherein said free flowing, inert powder is a water insoluble powder.

3. (original): A pellet as defined in claim 1 wherein said free flowing, inert powder is selected from the group consisting of microcrystalline cellulose, dicalcium phosphate, calcium sulfate, talc, an alkali metal stearate, silicon dioxide and calcium carbonate.

4. (original): A pellet as defined in claim 1 wherein the inner zone comprises from 0.1-95wt% of one or more pharmaceutically acceptable binders and or diluents and 99.9-5.0wt% of a biologically active agent.

5. (original): A pellet as defined in claim 1 wherein said outer zone is formed from a powder which forms a non-tacky surface when placed in contact with water and from 0.1-99wt% of a biologically active agent.

6. (original): A pellet as defined in claim 1 wherein said outer zone is formed from a powder comprising microcrystalline cellulose and from 0.1-99wt% of a biologically active agent.

7. (original): A pellet as defined in claim 1 wherein said inner zone additionally comprises one or more components selected from the group consisting of lubricants, disintegrants, flavors, surfactants, anti-sticking agents, osmotic agents and mixtures thereof.

8. (original): A pellet as defined in claim 1 wherein said outer zone additionally comprises one or more components selected from the group consisting of binders, diluents, disintegrants, lubricants, flavors, surfactants, anti-sticking agents, osmotic agents and mixtures thereof.

9. (original): A pellet as defined in any one of claims 1 or 2 wherein said inner or outer zone comprises a swellable matrix forming polymer.

10. (original): A pellet as defined in any one of claims 1 or 2 wherein said inner or outer zone comprises a non-swellable matrix forming polymer.

11. (original): A pellet as defined in any one of claims 1 or 2 wherein said pellet is provided with a layer comprising a swellable matrix forming polymer and a non-swellable matrix forming polymer.

12. (original): A pellet as defined in any one of claims 1 or 2 having one or more layers which comprise a release rate controlling polymer.

13. (original): A pellet as defined in any claim 8 wherein said swellable polymer is selected from the group consisting of hydroxypropyl methyl cellulose, hydroxypropyl cellulose, hydroxyethyl cellulose and carboxypolymethylene.

14. (original): A pellet as defined in any claim 11 wherein

said release rate controlling polymers are selected from the group consisting of ethyl cellulose, methacrylic acid copolymers, cellulose acetate phthalate, hydroxypropylmethylcellulose phthalate, hydroxypropylmethylcellulose acetate succinate, cellulose acetate trimellitate and polyvinyl acetate phthalate.

15. (original): A process for making pharmaceutical pellets as defined in claim 1 wherein said core or at least one of said layers is formed by (a) contacting powder particles, adhering them to each other and compacting said adhered pellets by a rolling movement, wherein the degree of densification is controlled by the rolling movement; and (b) feeding a sufficient amount of a substantially dry, free flowing inert powder which forms a non-tacky surface when placed in contact with water to provide on said particles an outer zone comprising a layer formed from said substantially dry, free flowing inert powder.

16. (original): A process for making solid pellets which are adapted for use as a pellet core for a dosage form which includes a biologically active agent, said process comprising:

(a) forming a powder mixture which comprises a binder and a biologically active agent;

(b) feeding said powder mixture which is optionally pre-wetted with from 0-60% of a pharmaceutically acceptable diluent, based on the total weight of the powder and the pharmaceutically acceptable diluent, to an operating apparatus which comprises a rotor chamber having an axially extending cylindrical wall, means for passing air through said chamber from the bottom, spray means for feeding a liquid into said chamber, a rotor which rotates on a vertical

rotor axis, said rotor being mounted in said rotor chamber, said rotor having a central horizontal surface and, in at least the radial outer third of said rotor, the shape of a conical shell with an outward and upward inclination of between 10° and 80°, said conical shell having a circularly shaped upper edge which lies in a plane which is perpendicular to the rotor axis, feed ports for introducing said powdered excipient, a plurality of guide vanes having an outer end affixed statically to said cylindrical wall of said rotor chamber above a plane formed by the upper edge of said conical shell of said rotor and an inner end which extends into said rotor chamber and is affixed tangentially to said cylindrical wall of said rotor chamber and having, in cross-section to the rotor axis, essentially the shape of an arc of a circle or a spiral, such that said powdered product which is circulated by kinetic energy by said rotor under the influence of kinetic energy, moves from said rotor to an inside surface of said guide vanes before falling back onto said rotor;

(c) rotating said rotor, while feeding air and spraying a pharmaceutically acceptable liquid into said rotor chamber for a sufficient amount of time to form solid pellets having a desired diameter; and

(d) feeding a sufficient amount of a substantially dry, free flowing inert powder which forms a non-tacky surface when placed in contact with water to provide on said particles an outer zone comprising a layer formed from said substantially dry, free flowing inert powder.

18. (original): A process as defined in claim 16 wherein in step (d) the dry powder has the same composition as the non-wetted powder that is fed in step (a).

18. (original): A process as defined in claim 16 wherein in step (d) the dry powder has a different composition from the composition that is fed in step (a).

19. (original): A process as defined in claim 16 wherein said powder mixture in step (a) comprises a biologically active agent and an inert powder that is selected from the group consisting of microcrystalline cellulose, dicalcium phosphate, calcium sulfate, talc, an alkali metal stearate, silicon dioxide, calcium carbonate and mixtures thereof.

20. (original): A process as defined in claim 16 wherein the powder mixture in step (a) comprises a biologically active agent and an inert powder that is microcrystalline cellulose.

21. (original): A process as defined in claim 16 wherein the biologically active compound is selected from the group consisting of vitamins, nutrients, pharmaceuticals and mixtures thereof.

22. (original): A process as defined in claim 16 wherein the biologically active agent is a pharmaceutically active compound.

23. (original): A process as defined in claim 16 wherein the pharmaceutically acceptable liquid diluent is water.

24. (original): A process for making discrete substantially spherical pellets comprising:

(a) feeding, a powder which comprises a biologically active agent and a binder, said powder being pre-wetted with from 5-60% of a pharmaceutically acceptable liquid diluent, based on the total weight of the powder and the liquid diluent, to an operating apparatus which comprises a rotor chamber having an axially extending cylindrical wall, means for passing air through said chamber from the bottom, spray means for feeding a liquid into said chamber, a rotor which rotates on a vertical rotor axis, said rotor being mounted in said rotor chamber, said rotor having a central horizontal surface and,

in at least the radial outer third of said rotor, the shape of a conical shell with an outward and upward inclination of between 10° and 80°, said conical shell having a circularly shaped upper edge which lies in a plane which is perpendicular to the rotor axis, feed ports for introducing said powdered excipient, a plurality of guide vanes having an outer end affixed statically to said cylindrical wall of said rotor chamber above a plane formed by the upper edge of said conical shell of said rotor and an inner end which extends into said rotor chamber and is affixed tangentially to said cylindrical wall of said rotor chamber and having, in cross-section to the rotor axis, essentially the shape of an arc of a circle or a spiral, such that said powdered product which is circulated by kinetic energy by said rotor under the influence of kinetic energy, moves from said rotor to an inside surface of said guide vanes before falling back onto said rotor; and

(b) rotating said rotor, while feeding air and spraying a pharmaceutically acceptable liquid into said rotor chamber for a sufficient amount of time to form substantially spherical pellets having a desired diameter; and

(c) feeding a sufficient amount of a dry powder which comprises a biologically active agent and a binder or a free flowing inert powder which forms a non-tacky surface in contact with water to form an outer layer on said substantially spherical pellets.

25. (original): A process as defined in claim 24 wherein in step (c) dry powder in an amount that is equivalent to 5 to 35 wt.% of the wetted powder that was initially fed to the apparatus, is added and the apparatus is allowed to run for a period of time to form said outer layer.

26. (original): A process as defined in claim 24 wherein said powder which comprising a biologically active agent includes microcrystalline cellulose and optionally comprises one or

more components selected from the group consisting of binders, diluents, lubricants, disintegrants, flavors, surfactants, anti-sticking agents, osmotic agents and mixtures thereof.

27. (original): A process as defined in claim 24 wherein the biologically active compound is selected from the group consisting of vitamins, nutrients, pharmaceuticals and mixtures thereof.

28. (original): A process as defined in claim 24 wherein the biologically active agent is a pharmaceutically active compound.

29. (original): A process as defined in claim 24 wherein the pharmaceutically acceptable liquid diluent is water.

30. (original): A pharmaceutical dosage form which comprises coated pellets having as a core a pellet as defined in claim 1 and one or more release rate controlling coatings selected from the group consisting of delayed release coatings and sustained release coatings or mixtures thereof.

31. (original): A pharmaceutical dosage form as defined in claim 30 wherein the controlled release coating is a sustained release coating.

32. (original): A pharmaceutical dosage form as defined in claim 30 wherein the controlled release coating is a delayed release coating.

33. (original): A pharmaceutical dosage form as defined in claim 30 wherein the dosage form includes different populations of coated pellets having different controlled release coatings.

34. (original): A pharmaceutical dosage form as defined in claim 30 wherein the dosage form is a hard gelatin capsule.